REMARKS

Claims 27-39 were pending in the application. Claims 27 and 31-33 have been amended. Claims 34 and 35 have been canceled. New claims 46-62 have been added. Accordingly, upon entry of the amendments presented herein, claims 27-33 and 36-62 will remain pending in the application.

Claims 27 and 33 have been amended to encompass an antibody or antibody binding fragment thereof which binds to an Fc receptor of an effector cell, wherein the binding to the Fc receptor (1) induces phagocytosis and lysis of the first cell and (2) is not blocked by endogenous ligand. Support for this amendment may be found, for example, in original claim 6, page 1 (lines 35-37); page 7, line 35 through page 8, line 3; page 24 (lines 5-13); and page 33 (lines 7-25) of the specification.

New dependent claims 36-63 have been added. Support for new claims 36-63 is available throughout the specification and claims as originally filed, as set forth below.

New Claim	Support
Claims 46-48	Original claims 17-18; page 2 (lines 10-21); and page 7 (lines 14-19).
Claims 49-50	Original claim 3; page 1 (lines 32-35); page 2 (lines 6-21); and page 14 (lines 31-34).
Claims 51-52	Original claim 4 and page 2 (lines 6-9).
Claim 53	Original claim 5; page 2 (lines 3-4); and page 22 (lines 12-13).
Claims 55-56	Original claim 6; page 2 (lines 4-6); and page 24 (lines 17-19).
Claims 57-58	Original claim 15 and page 21 (lines 9-10).
Claims 59-60	Original claim 16 and page 25 (lines 4-7).
Claim 61	Original claim 11; page 2, line 37 through page 3, line 2; and page 27 (lines 4-11).
Claims 62-63	Original claim 8.

No new matter has been added. Any amendment and/or cancellation of the claims should in no way be construed as an acquiescence to any of the Examiner's rejections and was performed solely in the interest of expediting prosecution of the application. Applicants reserve the right to pursue the claims as originally filed in this or a separate application(s).

Priority

The Examiner has requested that Applicants update the specification to reference the parent patent, U.S. Patent No.: 6,682,928 B2. Accordingly, Applicants have amended the specification as requested, thereby obviating this objection.

Rejection of Claims 27-34 and 39 Under 35 U.S.C. § 112, First Paragraph

Claims 27-34 and 39 are rejected as failing to comply with the written description requirement. Specifically, the Examiner alleges that "the specification does not provide sufficient description for any component or protein capable of binding to an Fc receptor other than an anti-Fc receptor antibody."

Applicants respectfully traverse this rejection. However, to expedite prosecution, independent claims 27 and 33 have been amended to specify that the component or protein capable of binding to an Fc receptor is an antibody (or antigen binding fragment thereof). Therefore, this rejection is moot.

Rejection of Claims 33 and 35-39 Under 35 U.S.C. § 112, First Paragraph

Claims 33 and 35-39 are rejected under 35 U.S.C. § 112, first paragraph, because according to the Examiner, "the specification, while being enabling for methods comprising the transformation of cells expressing a particular antigen *in vitro*, does not reasonably provide enablement for methods of transforming specific cells *in vivo*."

Applicants respectfully traverse this rejection. However, to expedite prosecution, independent claim 33 has been amended to incorporate the subject matter of claim 34, *i.e.*, to specify that transformation of the cell occurs *ex vivo*.

Rejection of Claims 35 Under 35 U.S.C. § 112, Second Paragraph

Claim 35 is rejected as being indefinite for depending from itself. Applicants have canceled claim 35, thereby rendering this rejection moot.

Rejection of Claims 27, 31-35 and 38-39 Under 35 U.S.C. § 102(a)

The Examiner has rejected claims 27 and 31-35 and 38-39 as being anticipated by Ledbetter *et al.* (WO 97/20048, June 5, 1997). The Examiner relies on Ledbetter *et al.* as teaching

> the construction of recombinant expression vectors which comprise a fusion protein comprising a single chain Fv molecule operatively linked to a transmembrane domain of a cell surface receptor and the use of said vector to transfect cells in vitro/ex vivo (Ledbetter et al., pages 6-7, page 12, lines 14-20, and page 21). Ledbetter et al. further teaches that the single chain Fv binds FcγR, Fcα, or FcεR, including CD64 which is FcγRI (Ledbetter et al., pages 6-7, bridging paragraph). Ledbetter et al. further teaches that the transfected cells expressing the single chain Fv fusion protein on the cell surface can be used in ex vivo or in vivo methods for enhancing a T cell response in a subject (Ledbetter et al., page 12). In particular, Ledbetter et al. teaches that autologous or allogeneic cells, such as tumor cells, are genetically modified to produce the sFV on the cell surface ex vivo and then administered to the subject to stimulate a T cell response (Ledbetter et al., page 12, lines 20-30).

Applicants respectfully traverse the foregoing rejection. As amended, independent claims 27 and 33 are drawn to methods of increasing an immune response using a cell transformed to express an anti-Fc receptor antibody which is not blocked by endogenous ligand. The transformed cell further induces phagocytosis or lysis of the cell.

Ledbetter *et al.* fail to teach or suggest the use of an anti-Fc receptor antibody (or fragment thereof) that binds outside (*i.e.*, is not blocked by) the endogenous ligand as a component for inducing phagocytosis or lysis of cells. Indeed, Ledbetter *et al.* neither teach nor suggest their expression vectors induce phagocytosis or lysis of cells, as presently claimed. Instead, Ledbetter *et al.* teach "mammalian cells which are genetically modified to express modified sFV molecules to its cell surface thereby *providing a co-stimulatory molecule* for the PBLs [peripheral blood leukocytes]" so that the PBLs can "*stimulate a T cell response*" (emphasis added) (see page 12, lines 13-19 of Ledbetter *et al.*). Essentially, Ledbetter *et al.* teach "modified sFV molecules which serve[s] as artificial *adhesion* receptors" to mediate "*adhesion* between lymphocytes...and between lymphocytes and non-lymphocytic cells" (emphasis added) (see page 6, lines 11-14 of Ledbetter *et al.*).

Thus, importantly, Ledbetter *et al.* fail to teach or suggest a method of increasing an immune response in a subject, as claimed by Applicants (*i.e.*, phagocytosis and lysis) and, instead, teach a composition for modulating an entirely different arm of the immune system.

As such, the pending claims are novel over Ledbetter *et al.* and Applicants respectfully request the Examiner to reconsider and withdraw this rejection.

Rejection of Claims 27-30 Under 35 U.S.C. § 103(a)

Claims 27-30 are rejected as being unpatentable over Ledbetter *et al.* in view of Fanger *et al.*, (WO 91/00360, January 10, 1991). The Examiner relies on Ledbetter *et al.* for the reasons discussed above, but acknowledges that "Ledbetter differs from the instant invention by not teaching the administration of an agent to increase the expression of Fc receptors on effector cells." The Examiner alleges that "Fanger et al. supplements Ledbetter et al by teaching that in related method of inducing immune responses by targeting effector cells with an antibody that binds to the Fc receptor, it is useful to pretreat the effector cells, such as macrophages, with IFN-gamma and/or TNF, IL-2 and colony stimulating factor." The Examiner furthers alleges that "Fanger et al. provides motivation for treating the effector cells with IFN-gamma or other cytokines by teaching that IFN-gamma increases the number of Fc receptors for attachment to the targeting antibody and that cytokines such as TNF further activate the effector cell (Fanger et al., page 10)."

Applicants respectfully traverse this rejection. As discussed in detail above, the primary reference, Ledbetter *et al.* fail to teach or suggest the claimed invention, *i.e.*, a method for increasing an immune response in a subject by inducing phagocytosis or lysis of the cell using an anti-Fc receptor antibody (or fragment thereof) that binds outside the natural ligand. Fanger *et al.* fail to make up for this deficiency. Although Fanger *et al.* teach the use of cytokines to activate effector cells, as well as antibodies which bind at an epitope on the Fc receptor which is distinct from the ligand binding site of the receptor, Fanger *et al.* do not teach or suggest the particularly claimed methods, *i.e.*, methods which encompass a cell transformed to express on its surface an anti-Fc receptor antibody of an effector cell such that the binding induces phagocytosis and lysis of the cell.

In view the foregoing, it is evident that Ledbetter *et al.* and Fanger *et al.*, either alone or in combination, fail to teach or suggest the present invention. Accordingly, Applicants

respectfully submit that the Examiner has failed to establish a *prima facie case* of obviousness and request that this section 103(a) rejection be reconsidered and withdrawn.

Rejection of Claims 33 and 36-37 Under 35 U.S.C. § 103(a)

Claims 33 and 36-37 are rejected as being unpatentable over Ledbetter *et al.* in view of Guyre *et al.* (*Cancer Immunol Immunother.* 1997 Nov-Dec;45(3-4):146-8). The Examiner relies on Ledbetter *et al.* for the reasons discussed above, but acknowledges that "Ledbetter et al. does not specifically teach the H22 antibody which recognizes CD64." The Examiner alleges that "Guyre et al. supplements Ledbetter et al. by teaching the H22 antibody and its use in generating fusion proteins with gp120 or tetanus toxin" and "provides motivation for using the H22 antibody in the single chain fusion protein taught by Ledbetter et al. by teaching that the H22 antibody binds to CD64 outside the ligand-binding domain of the receptor such that binding of H22 is not inhibited by serum IgG."

Applicants respectfully traverse this rejection. As discussed in detail above, the primary reference Ledbetter *et al.* do not teach or suggest the claimed invention. Guyre *et al.* fail to make up for this deficiency. Although Guyre *et al.* teach an antibody which binds outside the ligand-binding domain of FcγRI, as well as the use of cytokines to activate effector cells, Guyre *et al.* do not teach or suggest the particularly claimed methods, *i.e.*, methods for increasing an immune response in a subject by inducing phagocytosis and lysis of the cell using an anti-Fc receptor antibody (or fragment thereof) that binds outside the natural ligand.

In view the foregoing, it is evident that Ledbetter *et al.* and Guyre *et al.*, either alone or in combination, fail to teach or suggest the present invention. Accordingly, Applicants respectfully submit that the Examiner has failed to establish a *prima facie case* of obviousness and request that this section 103(a) rejection be reconsidered and withdrawn.

CONCLUSION

In view of the above amendments and remarks set forth above, it is respectfully submitted that this application is in condition for allowance. If there are any remaining issues or the Examiner believes that a telephone conversation with Applicants' Attorney could be helpful in expediting prosecution of this application, the Examiner is invited to call the undersigned at (617) 227-7400.

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Respectfully submitted,

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